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United States
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Minutes

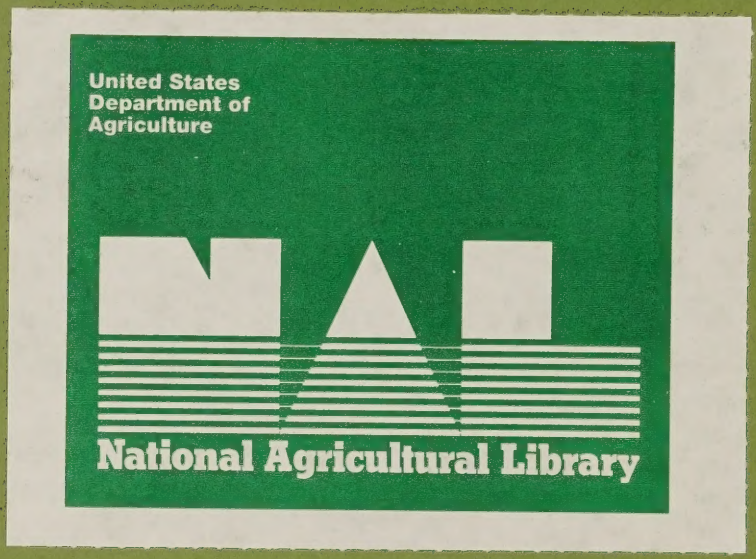
Agricultural Biotechnology Research Advisory Committee

Definitions Working Group
July 28, 1988

Research Guidelines
Working Group

July 28-29, 1988

Document No. 88-WG-02 and 03


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U.S. Department of Agriculture
Agricultural Biotechnology Research Advisory Committee

Working Group on Definitions
Minutes of Meeting
July 27, 1988

The Agricultural Biotechnology Research Advisory Committee (ABRAC), Working Group on Definitions was convened for its second meeting on July 27, 1988 in Washington, D.C. Dr. Edward L. Korwek chaired the meeting. The meeting was open to the public and announced in the Federal Register. For a complete list of those present see Attachment I.

In his opening remarks Dr. Korwek explained that he had not received guidance from the other Working Groups regarding which definitions were needed, therefore, he had selected words that were important and appeared frequently in the draft of the United States Department of Agriculture (USDA) "Guidelines for Research Outside the Laboratory Involving Biotechnology" (Henceforth referred to as the Guidelines). He stated that the Working Group should not strive for perfection, but rather decide on workable and publishable definitions which would provide a basis for feedback.

I. BIOTECHNOLOGY

After explaining that he had asked each of the Working Group members to develop definitions for certain terms, Dr. Korwek turned the floor over to Ms. Hollander to propose a definition of "Biotechnology."

Ms. Hollander described that her approach to developing definitions had, after considering other options, narrowed quickly to making small changes, if necessary, to the already widely accepted definitions in the 1986 U.S. Coordinated Framework. She therefore proposed:

> "Biotechnology is the application of biological systems and organisms to technical and industrial processes."

The Working Group then discussed the ramification of very general, broad definitions versus specific, detailed definitions. Dr. Kung stated that he preferred simple, short definitions which people would use. Dr. Korwek pointed out that a broad definition would serve as a base, to be further elaborated upon during the development of the Guidelines. He stated that, in the case of "Biotechnology," the proposed definition would perhaps not end up including every technology, for example the containment section of the Guidelines might exclude classical techniques. Ms. Hollander concurred with this approach, noting that it shifts the decision making to those who are dealing with risk assessment.

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By consensus the Working Group decided to define all terms broadly, often working from definitions which have already been accepted by one or more U.S. government agencies. These broad definitions would not necessarily lead to a broad oversight, because specific exceptions or limited oversight might be adopted for techniques using low, if any, risks.

Dr. Kemp disagreed with this approach, stating that the proposed definition for "biotechnology" was not really a definition at all because it includes everything. He said that the Working Group needed to be very careful because such a definition would set ABRAC's responsibility very widely.

Mr. Bothast inquired whether by starting broad and narrowing later, the process would achieve workable results? Dr. Korwek stated that success of the Recombinant DNA Advisory Committee proves that the broad to narrow approach is valid. Although Recombinant DNA is defined broadly, in fact, very few experiments are subject to the NIH Guidelines, as most are exempted because of lack of safety concerns.

Dr. Miller interjected that the Food & Drug Administration (FDA) favored the proposed definition because of its simplicity and because it was neutral, which is scientifically defensible.

The proposed definition (for a list of final definitions see Attachment II) was passed by a vote of 4 yeas and 1 nay.

II. BIOTECHNOLOGY RESEARCH

Dr. Korwek called on Dr. Kung to present his proposed definition. He stated, that, choosing between the various alternatives provided by Dr. Korwek, he preferred the USDA Office of Agricultural Biotechnology's (OAB) definition for "Biotechnology Research," "The endeavor to discover, develop, or verify research using non-classical biotechnology procedures to cause genetic variation in living organisms through the manipulation of heritable information." "Biotechnology research" and "research," when used in these guidelines, have the same meaning."

Dr. Korwek stated that the definition was circular since it used the word "research" to define "research." Ms. Hollander stated that she disagreed with using the term "non-classical." Dr. Kemp agreed that the definition had a lot of problems.

Dr. Kung then proposed a second definition, translated from the Chinese, "Research is a systematic investigation of a subject; in science, the effort to discover or develop a new product or process." Dr. Korwek stated that he liked the beginning of this definition, but it left open the issue of where research ends and product development begins.

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Dr. Kung then offered a third definition, based on the Working Group's comments, and a definition of research read by Dr. Langston from the Webster's Collegiate Dictionary.

> "Biotechnology Research is the endeavor to discover, develop or verify knowledge utilizing biotechnology."

Dr. Bothast questioned when the Working Group would begin to get specific, and warned that if the definitions continued to be too general, the opportunity to focus would be lost. Dr. Korwek and Ms. Hollander responded that how and when to focus is a risk assessment question.

The third definition, proposed by Dr. Kung was put to vote and passed unanimously.

III. ORGANISM

Dr. Korwek turned the floor over to Dr. Kung to offer his proposed definition of "organism." Dr. Kung said he liked the definition "any biologicai entity, cellular or non-cellular, with capacity for self-perpetuation and response to evolutionary forces; includes plants, animals, fungi, protists, prokaryotes, and viruses," except, "viruses" should not be included because they are not organisms. Dr. Kung also stated that he preferred the definition to be scientifically correct but if viruses were included, why not viroids, which were scientifically speaking also not organisms? Dr. Kemp proposed that "viroids" be added.

Dr. Langston said she preferred to include "viruses" and "viroids" because they must fit into some category and in common usage they are considered organisms. Dr. Korwek stated that the discussion raised the issue of scientific definitions, versus definitions useful for a particular purpose. Definitions don't have to be scientifically accurate; they can merely spell out what is covered.

Ms. Hollander pointed out that "includes" means "includes but is not limited to." She said she was against changing accepted definitions more than necessary, however, she could accept adding "viroids" and "includes but not limited to" to this definition. Dr. Bothast wondered if the term "prokaryotes" made sense in this list. The following definition passed unanimously:

> "An organism is any biological entity, cellular or noncellular, with the capacity for self-perpetuation and response to evolutionary forces; includes, but is not limited to plants, animals, fungi, protists, prokaryotes, viruses, and viroids."

IV. MICROORGANISM

Dr. Korwek gave the floor to Dr. Kung to propose a definition for "microorganism." Dr. Kung stated that he preferred,

> "A microorganism is an organism having microscopic or submicroscopic forms."

Dr. Korwek concurred, stating that he preferred Dr. Kung's proposed definition to the other possibility, "an organism that is a fungus, prokaryote, protist or virus" because Dr. Kung's proposed definition was more encompassing than the second definition.

Dr. Bothast agreed with Dr. Kung's proposal, and said there was no need to change the standard definition.

The definition proposed by Dr. Kung was put to a vote. It was passed unanimously. (See Part XIII Addendum on Microorganism)

At this point Dr. Kung left the meeting and thus four voting members were present for the remainder of the meeting.

V. RELEASE INTO THE ENVIRONMENT/RESEARCH OUTSIDE THE LABORATORY

Ms. Hollander proposed, "any use not consistent with the practices specified in section _____." She added that the Environmental Protection Agency (EPA) and other agencies are in the process of changing their definition of this term. She also added that she was concerned with one potential problem raised by the approach. That is the Guidelines would use the phrase in such a way that the proposed definition would be circular.

Dr. Kemp said Ms. Hollander's approach was regulatory and may not be useful for definition purposes. He stated that "Release Into the Environment" means that one can do what he wants with it. He suggested substituting "not contained" according to the Guidelines for "not consistent with the practices."

Dr. Korwek stated that it was difficult to come up with a definition without knowing how the phrase would be used by other ABRAC Working Groups. He stated that the definition could certainly be revisited later, after others had a chance to do their work.

The definition

> "Release Into the Environment means any use not contained according to the practices specified in section(s)[ ]"

was passed unanimously.

VI. PLANT

Dr. Kemp proposed the definition, "multicellular organism characterized by eukaryotic cells surrounded by rigid cell walls, photosynthetic ability and embryonic development; members include mosses, liverworts, and vascular plants." He said he had dropped the parenthetical phrase "including most terrestrial crop plants as well as forest and ornamental species" in the interest of consistency.

Dr. Korwek asked if "eukaryotic" was redundant with "photosynthetic abilities." Dr. Kemp said no.

Dr. Korwek and Dr. Langston expressed the concern that plant parts such as pollen might not be covered by this definition. Dr. Korwek stated that regulation of plants versus plant parts was a containment issue. Dr. Kemp stated that he believed the proposed definition covers plant parts. He used as an analogy, an animal, stating that one doesn't say animal heads, animal legs, etc....

Ms. Hollander suggested they adopt the definition, but make a note for the record that the plant versus plant parts issue may need to be addressed later. She also raised the question as to where fungi would fit? She stated that this could be a case like "organism." In this definition "include" means "includes but not limited to."

Dr. Korwek asked if there are non-plant, non-animal, non-microscopic organisms?" Dr. Kemp answered yes, that fungi and algae do not fit into any of these three groups, however he commented that if they were added to the definition of plant, the definition would be unacceptable to most scientists. He stated fungi and algae would be addressed in the definition of prokaryote and eukaryotes.

Dr. Korwek and Ms. Hollander stated that the Working Group should advise the ABRAC and other Working Groups that instead of using, "animal, plant, and microorganisms," they should use "organism," so as to include fungi and algae. The Group by consensus decided to proceed to the definitions of "prokaryote" and "eukaryote" and vote on these definitions together with the definition of "plant."

VII. PROKARYOTES

Dr. Korwek asked Dr. Kemp to propose a definition. Dr. Kemp proposed, "a cell or organism lacking membrane-bound, structurally discrete nuclei and organelles; prokaryotes include bacteria, mycoplasmas, and blue-green algae."

He stated the inclusion of "mycoplasms" was important. Ms. Hollander suggested that in both this definition, and in the definition of "Organism," the Working Group substitute "examples include" for "includes" and take out the phrase "but is not limited to." The Working Group agreed to this by consensus.

VIII. EUKARYOTES

Dr. Korwek asked Dr. Kemp to propose a definition. He proposed:

> "A eukaryote is a cell or organism with a membrane-bound, structurally discrete nucleus and well developed cell organelles; examples include plants, animals, fungi, and protists."

A vote was taken on this definition as well as the following definitions:

> "A plant is a multicellular organism characterized by eukaryotic cells surrounded by rigid walls, photosynthetic ability, and embryonic development; examples include mosses, liverworts, and vascular plants."

> "A prokaryote is a cell or organism lacking membrane-bound structurally discrete nuclei and organelles; examples include bacteria, mycoplasms, and blue-green algae."

All three definitions were accepted unanimously.

IX. ANIMAL

Dr. Korwek asked Dr. Bothast to propose a definition for animal. Dr. Bothast proposed,

> "An animal is a multicellular organism composed of eukaryotic cells with ingestive nutrition and lacking rigid cell walls and photosynthetic ability; examples include coelenterates, flatworms, molluscs, segmented worms, arthropods, echinoderms, and vertebrates."

Dr. Kemp asked if anyone was aware of any recent comment on this standard definition? No one was.

Dr. Korwek asked why OAB had not adopted this definition for its official list. Dr. Jones replied OAB had changed it as a result of Arlington House discussions.

The proposed definition was put to vote. It passed unanimously

X. WEED/NOXIOUS WEED

Dr. Korwek asked Dr. Kemp to propose a definition. Dr. Kemp stated he was unhappy with the standard Animal and Plant Health Inspection Service (APHIS) definition because it used the notion of "foreign." Dr. Kemp suggested "a weed is a plant that poses a threat to health of humans, animals, or agricultural crops." He added that, pragmatically, each state defines independently what a "weed" is.

Dr. Korwek stated the National Institutes of Health (NIH) also had problems defining "weed" and he did not know what their current definition is. He therefore suggested deferring a decision on the definition.

Dr. Kemp offered to work on the definition further after learning about how NIH had defined "weed." Dr. Jones agreed to contact NIH to get this information.

By consensus the Group decided to defer its decision.

XI. PEST/PLANT PEST

Dr. Kemp stated he preferred, "an organism which can directly or indirectly cause disease or damage to any plants or parts thereof or any processed or manufactured or other products of plants," because it uses "organism" which the Group had already defined.

Dr. Langston commented that if the Working Group defines "pest," it may not have to define "weed." Drs. Kemp, Jones, and Bothast concurred that the definition of "pest" was closely related to the definitions of "weed" and "pathogen." Ms Hollander stated that perhaps the definition should be broader and include injury to health and environment and even products that were non-agricultural, for example, an insect or microbe that ate plastic.

Dr. Korwek stated that he believed plastic might not fall under the purview of the ABRAC. Ms. Hollander replied that it would because the National Environmental Policy Act (NEPA) would apply.
Ms. Hollander proposed:

> "A pest is any organism injurious to health, environment or products or activities valued by society."

Drs. Bothast and Kemp stated they liked this definition.

Dr. Korwek expressed doubt that such a definition would be useful. He stated that it leaves it up to the user to decide what is of value to society. He added that he believed the definition might be too

broad, since the Working Group did not know how it would be used, but he would go along because it was consistent with the other definitions.

Dr. Kemp stated that he would prefer, "adversely effects" rather than "injurious" because it was broader. Dr. Jones said it was important to discriminate between "can adversely effect" and "does adversely effect." Ms. Hollander stated that she was more comfortable with the narrower, "injurious."

The proposed definition was put to vote and passed with 3 yeas, 0 nays, and 1 abstaining.

XI. PATHOGEN

Ms. Hollander proposed the definition, "a virus or microorganism, including its viruses and plasmids, if any, that has the ability to cause disease in other living organisms, e.g., humans, animals, plants, and microorganisms."

Dr. Korwek stated that to be consistent the Working Group should substitute, "causes disease" for "has the ability to cause disease."

Dr. Langston noted that not only microorganisms cause disease but sometimes macroorganisms cause disease, for example, flukes. Dr. Jones responded that perhaps the Group should distinguish between "disease" and "infectious disease." Dr. Kemp suggested substituting "organism" for "microorganism." Ms. Hollander and Dr. Bothast concurred.

Dr. Korwek stated that the word "living" in front of organism could create an issue. He cautioned that if some scientists don't consider viruses to be "living," this definition might not cover a virus which causes disease in another virus. Ms. Hollander agreed with this concern and requested that a note be made to ABRAC on the question of "living."

Dr. Kemp suggested that by being too broad the Working Group was putting too much responsibility in the hands of local Institutional Biosafety Committees (IBC) and each committee would have to interpret these broad definitions.

Dr. Korwek suggested "condition" might be more useful than "disease." Dr. Kemp disagreed stating that in common usage, pathogens cause disease. Dr. Korwek asked that the word "disease" be brought to the ABRAC to see if it requires further definition.

Dr. Bothast proposed,

> "A pathogen is an organism that causes disease in other living organisms."

The definition was brought to vote and passed with 3 yeas, 0 nays, and one abstaining.

XII. AGRICULTURE

Ms. Hollander suggested the Group work from the EPA regulations which had defined "non-agricultural." She noted that the EPA regulations referred to microorganisms, but they could be adapted to ABRAC needs.

Dr. Kemp asked what the purpose of defining agriculture is? Is the Working Group trying to carve out the area of ABRAC overview or is the Group trying to develop a broad, usable definition?

Ms. Hollander suggested agriculture could be defined as "within the purview of USDA." Dr. Korwek noted that this would be consistent with the guidelines which referred to all projects supported by USDA.

Ms. Hollander proposed that the definition of agriculture be deferred until the next meeting to see if the ABRAC really needed it.

XIII. ADDENDUM ON MICROORGANISM

Dr. Bothast suggested that the discussion on the definition of "microorganism" be reopened to clarify it and make it more consistent.

Dr. Kemp proposed the definition be amended to read:

> "A microorganism is an organism having microscopic or submicroscopic forms for all, or a predominant part, of its life cycle; examples include fungi, prokaryotes, viruses, and viroids."

The definition was put to vote and passed unanimously.

XIV. OTHER BUSINESS

Dr. Korwek noted that the Minutes of the June 24, 1988 meeting of the Working Group on Definitions were incomplete and recommended that OAB take more complete minutes. He suggested the Recombinant DNA Advisory Committee Minutes should serve as a model. Ms. Hollander agreed and suggested that the Minutes be redone, particularly with regard to the decision of the Working Group at the June 24, 1988 meeting that the ABRAC might not cover items which were the responsibilities of other agencies. She recommended the recording of the last meeting be reviewed, so that the public record would be

accurate. Dr. Korwek added that once this is done the Working Group could reconsider and adopt the minutes for the June 24, 1988 meeting. The meeting was adjourned.

M Steinbock

MARTHA STEINBOCK
Rapporteur

Attachment I

LIST OF ATTENDEES
ABRAC WORKING GROUP ON DEFINITIONS
JULY 28, 1988 MEETING

Dr. Edward Korwek
Dr. Rodney Bothast
Dr. John Kemp
Dr. Shain-dow Kung
Ms. Anne Hollander

Ten guests were also present at the meeting.

DEFINITIONS DEVELOPED AT THE DEFINITIONS WORKING GROUP MEETING OF JULY 28, 1988

Biotechnology is the application of biological systems and organisms to technical and industrial processes.

Biotechnology Research is the endeavor to discover, develop, or verify knowledge utilizing biotechnology.

Release into the environment means any use not contained according to the practices specified in Section[s] _____.

Organism is any biological entity, cellular or noncellular, with the capacity for self-perpetuation and response to evolutionary forces; examples include plants, animals, fungi, protists, prokaryotes, viruses, and viroids.

Microorganism is an organism having microscopic or submicroscopic forms during all or a predominant part of its life cycle; examples include fungi, prokaryotes, viruses, and viroids.

Plant is a multicellular organism characterized by eukaryotic cells surrounded by rigid cell walls, photosynthetic ability, and embryonic development; examples include mosses, liverworts, and vascular plants.

Animal is a multicellular organism composed of eukaryotic cells with ingestive nutrition and lacking rigid cell walls and photosynthetic ability; examples include coelenterates, flatworms, molluscs, segmented worms, arthropods, echinoderms, and vertebrates.

Weed [Definition pending OAB follow-up with NIH Working Group on Definitions.]

Pest is an organism injurious to health, environment, or products or activities valued by society.

Pathogen is an organism that causes disease in other living organisms. [Question: Does "disease" need further definition?]

Prokaryote is a cell or organism lacking membrane-bound, structurally discrete nuclei and organelles; examples include bacteria, mycoplasmas, and blue-green algae.

Eukaryote is a cell or organism with a membrane-bound, structurally discrete nucleus and well-developed cell organelles; examples include plants, animals, fungi and protists.

AGRICULTURAL BIOTECHNOLOGY RESEARCH ADVISORY COMMITTEE
MEETING OF THE RESEARCH GUIDELINES WORKING GROUP
U.S. DEPARTMENT OF AGRICULTURE
ROOM 3109-SOUTH BUILDING

July 28-29, 1988

The meeting of the Agricultural Biotechnology Research Advisory Committee (ABRAC) Research Guidelines Working Group convened at 1:15 p.m., July 28, 1988 in Room 3109-South Building, U.S. Department of Agriculture, Washington, D.C., with Sue Tolin, chair. The meeting was open to the public and was announced in the Federal Register.

I. Introduction

The chair called the meeting to order. Members of the Working Group present were: Harold Hafs, F. William Whitmore, Lois Miller, A. David Kline, Anne K. Vidaver, George Hill, and Ronald Sederoff. The Office of Agricultural Biotechnology (OAB) was represented by Alvin Young, Director; Fred Kuchler; Paul Stern and Eva Russnak. There were approximately six visitors in attendance. Members of the Definitions working group, Edward Korwek, Rodney Bothast and John Kemp joined the meeting along with Martha Steinbock from OAB for the duration of the meeting on July 28.

II. Review Charge to Working Group

Dr. Tolin reviewed the charge from the June 23-24, 1988 meeting of ABRAC for this working group which was the classification of agricultural biotechnology experiments and the overall general format of the research guidelines.

Dr. Tolin stated that at the June meeting of ABRAC the decision was made not to publish the guidelines as regulations. She stated that in doing this, it changed the format of the current draft. A decision was made to divide into three working groups (Definitions, Research Guidelines and Biocontainment) which together would be responsible for developing a completed draft and making it available to ABRAC for the September meeting.

Dr. Tolin asked if there were any changes recommended in the draft minutes of the June 24, 1988 meeting of the Research Guidelines Working Group. No changes were recommended.

III. Review Reading List and Documents

Dr. Young discussed the distribution of pre-meeting information to the working group. He also summarized the development plan for the research guidelines and the proposed research handbook. He indicated that ABRAC would have an opportunity to review the handbook in conjunction with the guidelines. The plan is to publish both in the Federal Register after the September meeting of ABRAC.

IV. NIH-USDA Connection

Dr. Tolin gave an historical review and described the various documents provided to the Working Group as background for the USDA Guidelines. Document 59 is a copy of the most recent version of the National Institutes of Health (NIH) Guidelines in their entirety, in which Section III-A-3 states that Recombinant Advisory Committee (RAC) review and NIH approval is needed for "deliberate release into the environment of any organism containing recombinant DNA." Document 56 is the minutes of the February 2, 1987 NIH RAC meeting in which the concept of developing appendices describing "accepted scientific practices" for planned introductions into the environment was initially developed. Document 58, referred to as the draft Science and Education (S&E) Guidelines, was the result, in part, of the USDA Workshop held December 1986 in Arlington, Virginia. This document included only certain appendices from the total draft, namely those describing conditions for conducting research with plants and animals, both within and outside of laboratories. Document 40, together with its summary in Document 41, present containment conditions for conducting research with plants (Appendix P) and animals (Appendix Q) that were developed from parts of Document 58 by NIH-RAC and their working groups and that, with modifications approved by RAC at their September 1987 meeting, are pending inclusion in the next version of the NIH Guidelines. In response to a question, Dr. Tolin stated that, by title and definition, the NIH Guidelines apply only to "Research Involving Recombinant DNA Molecules" and thus make no attempt to define biotechnology or include any techniques that do not use recombinant DNA methods.

Dr. Tolin presented a summary of the NIH Guidelines, particularly with respect to classification of experiments (Section III) and assignment of recommended containment levels (Biological Safety Levels 1-4) for each type of experiment; and explained that the level of review, Institutional Biosafety Committee (IBC) to RAC, corresponds roughly to the containment level, and increases as the risk of the organism to human health increases. She also explained that it was traditional for the RAC to review all experiments of a certain class until they could, with confidence, assign a containment level to the work and pass review responsibilities to a lower level,

i.e., the IBC. "Release into the environment" experiments required RAC review not because of a recognized risk, but because no descriptions of conditions required for such experiments had been developed. She also explained that the factors considered by RAC in judging the risk of recombinant DNA research with a particular organism had been survivability, multiplication, dispersal, transfer of the recombinant molecule to another organism, and the potential for harmful effects to occur unexpectedly.

V. Working Group Activities and Priorities

In judging how the Research Guidelines Working Group should define and approach their task, Dr. Tolin stated that the final format was essentially optional. She suggested that since Section 400 of Document 16 was designed to deal with classification of experiments and the types of research that can be done under a specified containment, the Working Group should make revision of this section their top priority for the day. She said the Confinement Working Group will write Section 300, describing levels of confinement or containment, and that the Definitions Working Group will review Section 200 dealing with definitions and probably Section 100 on Scope and Applicability.

In Dr. Tolin's view this Working Group as well as the entire ABRAC would be responsible for the overall format, including the preamble and discussion of comments received by USDA on the June 26, 1986 Federal Register publication, "Coordinated Framework for Regulation of Biotechnology; Announcement of Policy and Notice for Public Comment."

Dr. Tolin announced that the document provided to the working group by Paul Stern was a revision of Document 16 provided to ABRAC at the June meeting. Mr. Stern explained that, since ABRAC had made the recommendation to develop guidelines rather than regulations, he had deleted mandatory language and incorporated minor suggestions made by the USDA, Office of General Counsel (OGC). Dr. Tolin clarified that since this document represented only minor changes from Document 16, it could be called Document 16A and used as a point of departure for this working group. To enable the group to concentrate on Section 400, Mr. Stern volunteered to look at the preamble section and provide a modified version of it as well as the complete guidelines for the ABRAC.

Dr. Young and Dr. Kuchler discussed the handbook currently in preparation. In their view, the guidelines would be relatively brief but the handbook would be more detailed and give an overall picture. Dr. Young stated that the intent is to provide it to the ABRAC for review because the content of the handbook and guidelines must ultimately be balanced.

At the conclusion of the Definitions Working Group, the chair, Dr. Korwek summarized the definitions for the benefit of the Guidelines Working Group since it was crucial to their further efforts. He said they agreed to define biotechnology simply and broadly, and that most of the definitions were developed from general definitions which are broad and inclusive.

Dr. Miller expressed concern that the definitions did not address research. She said a definition of biotechnology was adopted by federal agencies in 1986 with the intent of keeping it very broad. Dr. Vidaver suggested the definition in the recent Office of Technology Assessment (OTA) report might be an appropriate starting point as well. A visitor from a regulatory agency said some terms have statutory definitions and there will be problems if definitions in the guidelines differ from those.

VI. Developing a Classification of Experiments: Discussion

The working group agreed to begin with the classification of all experiments included in the broad definition of biotechnology.

It was agreed by consensus that the USDA guidelines should, as much as possible, parallel NIH guidelines with Dr. Hafs' suggesting 4 categories for experiments:

III-A. ABRAC review USDA/IBC approval.
III-B. IBC approval, B2, B3, B4; BL2, BL3 BL4
III-C. IBC notification BL-1, Classification 1
III-D. Exempt - B1 recommended.

It was agreed that in order to establish categories, we must define the organism; vector or construct, and containment, then figure out how to weight them relative to risk. In setting up a classification, the most stringent containment could be used for the highest risk. The Principal Investigator (PI) and the IBC would do the actual detailed description of containment, taking the principles established in the guidelines under advisement.

Once risk categories are established, then a specified level of confinement is recommended and specified procedures are used to achieve the level of confinement. In this way, guidelines are based on conditions for conducting experiments and not on who approves an experiment. The categories could be assigned by risk, e.g., uncertain, high, low and no risk. For example, Document 41 could be used as a basis for setting up categories of organisms based on their potential to cause disease and thus pose a risk.

Dr. Tolin asked the plant scientists (Drs. Whitmore and Sederoff), animal scientists (Drs. Hafs and Hill) and microbiologists (Drs. Miller and Vidaver) in the Working Group to take the science they

represent and to attempt to establish some categories during the evening recess.

She assigned to Dr. Kline the overall coordination on risk assessments--tying it in with documents 41, 58, 40.

Dr. Miller stressed that the group should be more concerned about differences between the traits of the original organism and the modified organism, than the nature of the organism itself.

Dr. Sederoff suggested that the basic premise of guidelines is to establish fundamental principles upon which many specific cases can be evaluated that transcend precise experiments and organisms. The Working Group endorsed this premise and agreed to proceed on this basis.

VII. Establishing Risk Categories: Principles

Dr. Hafs and Dr. Hill jointly reported that for animals the risk should not be based just on environmental and ecological safety but also human safety. If the proposed research in any way engenders any human risk, it should be assigned to the highest risk category. If no human risk is involved, then the evaluation should proceed to ecological and environmental risk. If there is any human risk at all, the experiment needs to be confined completely. A member of the group asked if you put uncertainty at highest risk. Dr. Hafs responded that they should adopt principles similar to NIH that if the risk to humans in vicinity of research is unknown, then it should be placed in the highest risk category.

Dr. Sederoff stated he liked the principles of human risk, ecological risk and uncertainty. Dr. Hafs said he liked the list from the RAC, as presented by Dr. Tolin which included survivability, multiplication, spread/dispersal, transfer of genetic information to another organism, and unexpected harmful effects. Dr. Hafs said the group needs to establish levels of risk.

Dr. Hafs said that his intent was that if there is real or apparent risk, an experiment should be placed at high risk with specific and appropriate protocols for protection of people working with the organism, and that care should be taken to do this at the time of establishing the protocol, and designing the safest way to conduct the research. Dr. Tolin suggested that levels could be a gradation from H1 to H4 (low to high), increasing stringency of operation as the risk for humans increases, and E1 to E4 for the environment with the realization that a different set of confinement procedures and principles should be developed. Dr. Hafs said the guidelines would instruct people--the researchers and principal investigators--to first ask about human risk, and then deal with the environmental and ecological risk.

Dr. Tolin said that with the proper information and understanding of the properties of the organisms and the environment, the guidelines could recommend straight forward, good common sense procedures. Dr. Miller added that the approach should be narrowed down to looking at relative risks.

Based on the discussions, Dr. Vidaver developed the following classifications and presented them to the working group:

I. Experiments Exempt from Review. Experiments to be conducted outside the laboratory with organisms genetically modified by selection from standard breeding practices, and somaclonal variation, organisms mutated by natural events, organisms containing randomly induced genetic changes equivalent to natural mutations (i.e., undirected mutation) and cells and/or embryo arising from fusions are exempt from all review requirements, except to the extent that appropriate local, state or federal statutes apply to the use of the unmodified organism. Such modified organisms are considered to have essentially no risk to humans, or to managed or natural ecosystems.

II. Experiments Requiring IBC Notification. Experiments to be conducted outside the laboratory with organisms genetically modified by biotechnological techniques that are the result of deletions, amplifications or genomic rearrangements made by recombinant DNA or other procedures, or with organisms that are essentially genetic equivalents of modified organisms previously approved by a Federal agency, require IBC notification, except to the extent that appropriate local, state or Federal statutes apply to the use of the unmodified organism. Such modified organisms are considered to have some potential for risk, but of predictably low consequence to human, managed or natural ecosystems.

III. Experiments Requiring IBC Approval. Experiments to be conducted outside the laboratory with organisms genetically modified by biotechnological techniques that are the result of insertions, whether coding or non-coding sequences, require IBC review and approval prior to initiation. The particular technique leading to such insertions may be based on biological or physical principles, including but not limited to somatic cell fusions, recombinant DNA, electroporation, etc. Such modified organisms are considered to have some recognized potential for risk, with low consequences to humans and managed or natural ecosystems. Local, state or federal statutes may apply to the use of both the modified and unmodified organism.

Dr. Miller made the following additions, which, together with the initial version, were approved unanimously by the Working Group. Part I, line 6, after "mutation", add "organisms containing directed mutations, including those genetically modified by recombinant DNA, e.g., simple deletions, simple point mutations, gene amplifications

or genomic rearrangements, that are essentially equivalent to those that are likely to occur naturally," Part II, line 4, insert "multiple" before "deletion, "complex" before "amplifications" and "genomic" and delete "made by recombinant DNA or other procedures." Part III insert "microinjection" before "etc."

Dr. Tolin summarized that knowing the procedure by which the organism was modified is important in the evaluation of risk; that the organism is important, as is the nature of the inserted gene and the trait; and that risk from the modified organism should be assessed relative to the non-modified organism.

She indicated the group needed to consider developing a fourth category: experiments that have recognized potential for high risk and that have to come to ABRAC. The Working Group generally agreed.

VIII. Guidelines that combine Risk Categories, Confinement Level, and Review of Experiments.

Dr. Sederoff said that releasing organisms into the environment, problems with agriculture, plants and animals, are going to be different from what NIH has done, and that ABRAC will have to decide what the levels of confinement are, the conditions of confinement, if the experiment should be approved, who approves it, and if approved what confinement would be appropriate.

Dr. Tolin recommended that the high risk confinement level be determined on a case-by-case basis and that each organism should be considered with its confinement level. Dr. Miller stated risk levels and then confinement levels could be developed, but confinement levels may not exactly correspond to the risk level depending upon what basic element of risk is involved.

Dr. Sederoff said there will be a spectrum of organisms and situations and thus the guidelines have to be flexible. Dr. Sederoff stated that the guidelines should state that the confinement must be appropriate to the risk and should be as precise as possible regarding confinement conditions. If this can't be done, then examples should be given. He stated that there is a well established principle that once you have defined the experiment and the risk, then you match the confinement conditions. Dr. Tolin stated that with any field experiment the confinement required could be from very low to very high depending on the organism and where it is placed in the risk evaluation.

Dr. Tolin said that by RAC precedent, a high confinement experiment probably needs a greater level of review because it is high confinement. She said that when there is a spectrum of confinement, then the review needs to be categorized as to the level of confinement that is recommended, as well as the level of review specified in the guidelines. Dr. Sederoff said that this needs to be

considered, but that it should not be determinative. Dr. Tolin said that if it is a high level of confinement, chances are a regulatory agency will be setting some of the confinement conditions and that the experiment will have federal review because of the nature of the organism. Dr. Sederoff said the Confinement group would have to define precisely what that confinement will be. Dr. Tolin commented that perhaps the confinement group could work on some spectrum of confinement for small-scale field tests.

Dr. Vidaver asked if the Guidelines Working Group could suggest to the Confinement Working Group how they might define small scale. Dr. Vidaver said perhaps they could downgrade from what has already been considered by other agencies and state that small-scale is one land acre or less. She did not know what it would be in water. Her suggestion goes back to EPA's originally exempting research for small-scale field tests that were under 10 acres on land and one acre in water. She said what ABRAC and the rest of the government is saying is that if an organism is made by recombinant DNA, they want to look at everything. She suggested that, if ABRAC went further down in plot size, researchers could conduct experiments at an intermediate level and then anything above that would be large-scale or something else.

Dr. Sederoff said the Confinement Working Group needed to think about defining the reasonable size of an experiment. He said it would be a good idea to have some small level of experiment that would be adequate for what most researchers want to do to obtain initial test results. Dr. Miller said there was only one experiment she could think of that should perhaps not be done at the small-scale level and that would be to test microbial pesticides. She did not know if they should concern themselves about this since EPA has regulatory authority for pesticides. Dr. Sederoff said it would be a great service to the scientific community if there were some small-scale category experiments which could be easily done with local IBC approval. Dr. Vidaver said that since the whole idea was to have everything coordinated, ABRAC could suggest criteria for adoption. Dr. Vidaver said ABRAC could suggest that small is one acre or less, intermediate would be one to 10 acres, and then the large-scale would require some super approval or something of that nature. Dr. Sederoff said that some definition of scale would at least let small research experiments that are well contained be conducted with fewer criteria than those normally used.

Dr. Tolin asked if that meant defining a level four confinement under which an experiment could be conducted with just IBC approval. She said if a researcher wanted to go to a lower level of confinement, which would be an increase in scale or less containment, then they would have to get federal approval. Thus the approval level would go up as the confinement is decreased.

Dr. Sederoff said there was a concept there that he liked. He said that it implies that confinement and approval are related, and that

if you have maximum level of confinement, it is safe for anything because it is so highly confined. This would mean a researcher could do any experiment without anyone's approval if it is done at the highest confinement level.

Dr. Tolin stated that this concept appears to reverse the concept that the higher the containment, the higher the risk, and thus the higher level of approval needed. The group agreed that this idea should be brought to the ABRAC for further discussion after confinement levels are developed by that working group. Dr. Sederoff said that the higher the containment used, the easier it should be for researchers to do their experiment. Dr. Tolin said that was the principle, but if they were doing a very highly contained field experiment she felt they should at least notify their IBC. She said if they wanted to decrease the containment then they needed to get their IBCs approval before they do it.

Dr. Vidaver said that they should be very cautious as to how they consider confinement extremes. Dr. Sederoff said there was still a way the guidelines could address small-scale experiments. It should be possible to specify some moderately high level of confinement that would allow the researcher to do small pilot experiments.

Dr. Tolin's final charge to the group was to go back and reread Documents 60, 61 and 58 now that the Group had the benefit of the discussion, and get written material to OAB prior to the Confinement Working Group meeting. She stated that material must be received in OAB by August 8, 1988 and that she would be attending the Confinement Group meeting to convey the results of the Guidelines Working Group discussions to them.

Fred Kuchler and Eva Russnak were asked to draw together a document, based on the meeting and come up with a draft report prior to the August 11-12, 1988 meeting of the confinement working group.

Meeting adjourned at 3:20 p.m., July 29, 1988.

Eva Russnak

EVA RUSSNAK
Rapporteur

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